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REMARKS/ARGUMENTS

Original method claims 1-5 have been cancelled and replaced by new method claims 10-14, and withdrawn apparatus claims 6-9 remain in the application pending the filing of a divisional application on the invention thereof.

The Applicant courteously contends that the invention recited in the amended claims is clearly patentably distinguishable from the teachings of the cited prior art.

According to Applicant's invention, an improved method of growing cells is achieved, in which multiple sources of nutrient media, of growth factors and ventilation gases are provided to feed the enclosure containing the cells with mixtures of nutrient media, mixtures of growth factors and mixtures of ventilation gases which are determined to be appropriate for a particular application, and wherein the compositions and the flow rates of the different mixtures may be modified during the progress of the application, these modifications being effected independently of each other.

As explained in the specification, this method presents a number of advantages, including:

- (a) it can be used as a research tool and for clinical applications, for example to grow cells taken from a patient or a donor;
- (b) it can be used with growth chambers of different volumes;
- (c) it can be used for a plurality of different applications;
- (d) the composition and the quantity of growth factors delivered to a bioreactor may be adjusted and varied as necessary, which is very important in a continuous or discontinuous perfusion growth system;
- (e) the composition and the quantity of nutrient medium and of ventilation gases may be adjusted and varied at will; and
- (f) the method increases the yield from a bioreactor and enables a same type of bioreactor to be used for different applications.

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Such a method is neither disclosed nor suggested by the cited references.

The Fei, et al., U. S. patent No. 5,635,387 relates to methods and device for culturing human hematopoietic cells and their precursors, the culture medium comprising a nutritive medium, a source of growth factor, and optionally containing a source of plasma or serum. However, the compositions and the flow rates of the nutritive medium and of the growth factors which are delivered to the cells cannot be varied and modified at will during the progress of the application.

Hopkins U. S. patent No. 4,468,455 discloses a cell culture wherein a given additive is added to a nutrient medium after determination that the cell culture is in a condition to be able to use the additive effectively. This process permits to increase the metabolic activity of a particular cell culture. It can be used only for a particular type of cell culture and it cannot be used for multiple applications such as maintenance, proliferation, amplification or differentiation of cells, because it does not comprise any steps of selecting compositions and flow rates of mixtures of different nutrient media supplied from multiple sources of nutrient media.

The same remarks apply also to the other prior documents cited by the Examiner. More particularly, the Vajta U. S. patent No. 6,399,375 discloses a method of culturing cells into sealed bags immersed into a liquid bath. No means are provided to deliver variable compositions and flow rates of nutrient media, growth factors and gases into the bags during the culture;

In the Emerson, et al., U. S. patent No. 5,646,043, methods are taught for the ex-vivo replication of human cells and/or expansion of human progenitor cells. The culture medium comprises a nutrient medium, which nutrient medium is replaced at high rate. However, there is only one source of nutrient medium and no means are provided for varying the compositions and the flow rates of the media during the progress of the culture;

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The Takeuchi, et al., U. S. patent No. 5,304,483 relates to a process for controlling cultivation conditions for animal cells, by the control of the dissolved oxygen concentration and/or glucose concentration in the culture medium. This document is focused on the control of oxygen or glucose and does not disclose any means for varying the compositions and the flow rates of nutrient media or growth factors injected in the culture;

The Kearney U. S. patent No. 5,424,209 discloses an automated cell culture and testing system which is microgravity adapted. The system is self-contained and comprises a plurality of independent bioreactors, a source of nutrient medium and a plurality of sources of testing media. No means is provided for varying the composition of the nutrient media. Further, no means is provided for varying the compositions and flow rates of growth factors and ventilation gases;

The Palsson, et al., U. S. patent No. 5,888,807 discloses devices for maintaining and growing human stem and/or hematopoietic cells. Diverse cell types are simultaneously cultured, but no means are provided to modify the compositions and flow rate of the liquid medium containing nutrients, growth factors and other chemical compounds which is supplied to the culture chamber. Only the global rate of perfusion in the culture chamber will vary depending on the cell density;

The Grandics, et al., U. S. patent No. 5,571,720 teaches an integrated cell culture-protein purification system for the automated production and purification of proteins. There are no sources of different nutrient media and of growth factors in this system which is not a culture system but a purification system;

The Pykett, et al., U. S. patent No. 6,440,734 teaches methods and devices for the long-term culture of hematopoietic progenitor cells. The culture is set on a three-dimensional porous biomaterial, such as a porous solid matrix, without growth factors. No means are disclosed for selecting and modifying the composition of the nutrient media which is introduced into the culture chamber.

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Accordingly, Applicant courteously believes that the present invention is clearly patentably distinguishable from the cited prior art, and that allowance of the application is warranted.

Favorable action is courteously solicited.

Respectfully submitted,

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